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(71) Applicant *(for AE, AL, AM, AT, AZ, BA, BE, BF, BG, BJ, BR, BY, CF, CG, CH, CI, CM, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, FR, GA, GE, GN, GQ, GR, GW, HR, HU, ID, IS, IT, JP, KG, KP, KR, KZ, LC, LR, LT, LU, LV, MA, MC, MD, MG, MK, ML, MR, MX, NE, NL, NO, PH, PL, PT, RO, RU, SE, SI, SK, SN, TD, TG, TJ, TM, TN, TR, UA, UZ, VN, YU only)*: **UNILEVER N.V.** [NL/NL]; Weena 455, NL-3013 AL Rotterdam (NL).

(71) Applicant *(for AG, AU, BB, BZ, CA, CY, GB, GD, GH, GM, IE, IL, KE, LK, LS, MN, MW, MZ, NZ, OM, SD, SG, SL, SZ, TT, TZ, UG, ZA, ZM, ZW only)*: **UNILEVER PLC** [GB/GB]; UNILEVER HOUSE, Blackfriars, London, Greater London EC4P 4BQ (GB).

(71) Applicant *(for IN only)*: **HINDUSTAN LEVER LTD** [IN/IN]; HINDUSTAN LEVER HOUSE, 165 - 166 Backbay Reclamation, 400 020 Mumbai (IN).

(72) Inventors: **HALL, Peter, John**; 237 Spital Road, Bromborough, Wirral, Merseyside L62 2AF (GB). **LITTLEWOOD, David, Thomas**; Unilever Research Port Sunlight, Quarry Road East, Bebington, Wirral, Merseyside CH63 3JW (GB).

(74) Agent: **ROSEN JACOBSON, Frans**; Unilever Patent Department, Olivier van Noortlaan 120, Vlaardingen, Merseyside 3133 AT (GB).

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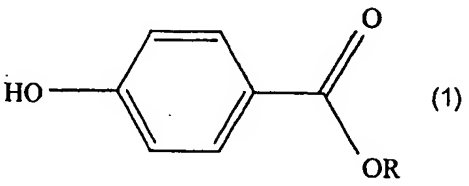
(54) Title: ORAL COMPOSITION COMPRISING AN ALKYLHYDROXYBENZOATE



(1)

(57) Abstract: Oral composition comprising:(a) an alkyl hydroxybenzoate represented by Formula (1): wherein R represents an alkyl group comprising at least five carbon atoms, and(b) said composition having an alkaline pH.

ORAL COMPOSITION COMPRISING AN ALKYLHYDROXYBENZOATE

COMPOSITION

The present invention relates to a composition comprising an alkyl hydroxybenzoate.

Alkyl hydroxybenzoates (parabens) are known in the art where the alkyl group is methyl. For example, methyl hydroxybenzoate is mentioned, albeit fleetingly, for use in medicinal and oral care preparations as a preservative (WO 00/09507 and WO 00/69401).

In addition, US 5 094 841 (Fine) discloses the use of heptyl paraben as a preservative in an oral care formulation. However, it also states that the preferred preservatives are methyl and propyl paraben and only ever states that they may be included in small amounts (0.1%) to provide a preservative effect.

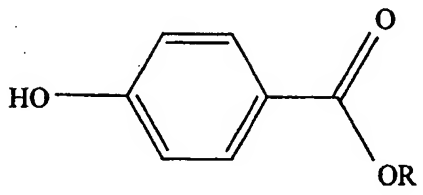
EP-A2-0 161 898 (Unilever) discloses the use of parabens in oral care, in particular, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, hexyl, heptyl and benzyl parabens.

We have surprisingly found that alkyl esters of para hydroxy benzoic acid can be formulated in an oral care composition with an alkaline pH and contrary to what would have been expected they do not hydrolyse significantly into the free alcohol and acid.

Accordingly, the invention provides oral composition comprising:

(a) an alkyl hydroxybenzoate represented by formula 1

Formula 1:



wherein R represents an alkyl group comprising at least five carbon atoms, and

(b) said composition having an alkaline pH.

The alkyl group of the compound according to Formula 1 is an alkyl comprising more than five carbon atoms. Preferably, the alkyl group comprises no more than 30 carbon atoms. More preferably the alkyl group comprises from 6 to 15 carbon atoms, especially from 6 to 10 and especially preferably, 7 or 8. These longer chain alkyl parahydroxy benzoic acids have never been considered before in alkaline environments because they were thought to be unstable.

Further, the alkyl group may be branched or straight chain and/or substituted or unsubstituted.

Preferred alkyl groups include octyl, heptyl and 2-ethylhexyl, more preferably, n-octyl or 2-ethylhexyl. Such compounds may be made by simple esterification of 4-

hydroxybenzoic acid with the respective alcohol. Such a process is a simple step for the person skilled in the art to carry out.

The most preferred alkyl groups on the alkyl para hydroxybenzoic acids are straight chain and include seven or, more preferably, eight carbon atoms.

The compound according to Formula 1 is preferably present in an amount such that an antibacterial effect can be provided. In practice this ranges from 0.15 to 20% by weight of the composition according to the invention. Preferably, in an amount ranging from 0.8 to 10% by weight and even more suitably from 1.0 to 3% by weight.

This surprising stability is particularly suitable for the longer chain alkyl parahydroxybenzoates, for example where the alkyl chain comprises at least seven carbons, especially preferably eight carbons in a straight chain and without wishing to be bound by theory it is thought that the longer chain parabens agglomerate to form micelles within the composition structure and thus protect each other from degradation in the alkaline environment. This effect is particularly surprising where chalk is used as an abrasive and the pH of the composition is thus much raised, from 8.5 to 11.5 being typical.

The oral composition according to the invention has an alkaline pH. This means that the pH of the composition is more than 7. Preferably, the pH of the composition is from 7.5 to 12, more preferably from 8 to 11, especially

preferably from 9 to 10. It is to be understood that any combination of any given bottom range limit with any given top limit can be used.

The oral composition according to the invention may comprise chalk as abrasive. Typically the term chalk is denoted to mean not just pure calcium carbonate but also ground marble. Chalk is usually in a crystallised form with many different types of crystals. For example, aragonite and calcite are two common crystal types. Further, natural chalk may also be used in oral care compositions. This natural chalk is commonly referred to as 'fine ground natural chalk' or FGNC.

Where FGNC is used it typically comprises particulate material of number average diameter ranging from 1 to 15 μm, preferably from 2 to 10 μm.

The chalk of the composition may even comprise a mixture of chalk types, e.g. precipitated calcium carbonate (PCC) plus FGNC, or even different types of FGNC.

Typically the amount of chalk present when used as an abrasive ranges from 1 to 60% by weight of the composition, preferably from 20 to 50% by weight.

It is to be understood that the oral composition according to the invention is capable of being used to clean the oral cavity, whether as part of a quotidian regime or as part of a one-off treatment. Typically oral care compositions comprise orally acceptable carriers. Further, oral compositions usually comprise oral care benefit agents

selected from the group consisting of anti-caries agents, anti-tartar agents, flavours, whitening agents, abrasives, bleaches and anti-malodour agents.

The oral composition according to the invention may also comprise bicarbonate as abrasive.

In another preferred embodiment the composition according to the invention comprises a surfactant. The surfactant is selected from the group consisting of anionic, non-ionic, cationic and zwitterionic surfactants or mixtures thereof and is present in the composition in an amount ranging from 0.01 to 5% by weight, preferably from 0.1 to 2.5% by weight and especially preferably from 0.5 to 1.8% by weight of the composition. Preferred surfactants include the anionic surfactants, in particular the alkali-metal alkyl sulphates, e.g. sodium lauryl sulphate.

The oral composition according to the invention may also comprise further ingredients which are common in the art, such as:

antimicrobial agents, e.g. Triclosan, chlorhexidine, copper-, zinc- and stannous salts such as zinc citrate, zinc sulphate, zinc glycinate, sodium zinc citrate and stannous pyrophosphate, sanguinarine extract, metronidazole, quaternary ammonium compounds, such as cetylpyridinium chloride; bis-guanides, such as chlorhexidine digluconate, hexetidine, octenidine, alexidine; and halogenated

bisphenolic compounds, such as 2,2' methylenebis-(4-chloro-6-bromophenol);

anti-inflammatory agents such as ibuprofen, flurbiprofen, aspirin, indomethacin etc.;

anti-caries agents such as sodium- and stannous fluoride, aminefluorides, sodium monofluorophosphate, sodium trimeta phosphate and casein;

plaque buffers such as urea, calcium lactate, calcium glycerophosphate and strontium polyacrylates;

vitamins such as Vitamins A, C and E;

plant extracts;

desensitising agents, e.g. potassium citrate, potassium chloride, potassium tartrate, potassium bicarbonate, potassium oxalate, potassium nitrate and strontium salts;

anti-calculus agents, e.g. alkali-metal pyrophosphates, hypophosphite-containing polymers, organic phosphonates and phosphocitrates etc.;

biomolecules, e.g. bacteriocins, antibodies, enzymes, etc.;

flavours, e.g. peppermint and spearmint oils;

proteinaceous materials such as collagen;

preservatives;

opacifying agents;
colouring agents;

pH-adjusting agents;

sweetening agents;

pharmaceutically acceptable carriers, e.g. starch, sucrose, water or water/alcohol systems etc.;

particulate abrasive materials such as silicas, aluminas, calcium carbonates, dicalciumphosphates, calcium pyrophosphates, hydroxyapatites, trimetaphosphates, insoluble hexametaphosphates and so on, including agglomerated particulate abrasive materials, usually in amounts between 3 and 60% by weight of the oral care composition.

humectants such as glycerol, sorbitol, propyleneglycol, xylitol, lactitol etc.;

binders and thickeners such as sodium carboxymethyl-cellulose, xanthan gum, gum arabic etc. as well as synthetic polymers such as polyacrylates and carboxyvinyl polymers such as Carbopol®;

polymeric compounds which can enhance the delivery of active ingredients such as antimicrobial agents can also be included;

buffers and salts to buffer the pH and ionic strength of the oral care composition; and

other optional ingredients that may be included are e.g. bleaching agents such as peroxy compounds e.g. potassium peroxydiphosphate, effervescing systems such as sodium bicarbonate/citric acid systems, colour change systems, and so on.

Liposomes may also be used to improve delivery or stability of active ingredients.

The oral compositions may be in any form common in the art, e.g. toothpaste, gel, mousse, aerosol, gum, lozenge, powder, cream, etc. and may also be formulated into systems for use in dual-compartment type dispensers.

Embodiments according to the invention shall now be discussed with reference to the following non-limiting examples.

EXAMPLE

The following formulation is a composition according to the invention and is made by ordinary methods known to a skilled person.

Ingredient	w/w%
Fine ground natural chalk	40

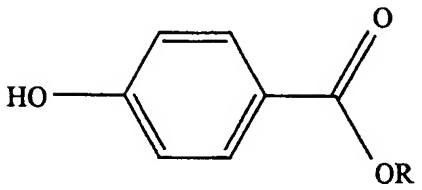
Sorbitol (70%aq)	25
Sodium lauryl sulphate	2.5
sodium monofluorophosphate	1.1
octyl parahydroxybenzoic acid	1.0
sodium carboxy methyl cellulose	0.9
trisodium phosphate	0.3
flavour	1
water	to 100

This octyl parahydroxy benzoic acid in this formulation was stable at 37°C for two months.

CLAIMS

1. Oral composition comprising

(a) an alkyl hydroxybenzoate represented by formula 1



Formula 1:

wherein R represents an alkyl group comprising at least five carbon atoms, and

(b) said composition having an alkaline pH.

2. Composition according to claim 1, wherein R represents an alkyl group comprising from six to fifteen carbon atoms.

3. Composition according to claim 1 or 2, wherein R represents an alkyl group comprising from seven to ten carbon atoms.

4. Composition according to claims 1 to 3, wherein R represents a group selected from the group consisting of octyl and heptyl.

5. Composition according to any of claims 1 to 4, wherein R represents a branched alkyl group.

6. Composition according to any of claims 1 to 4, wherein R is a straight chain alkyl group.

7. Composition according to claims 1 to 5, wherein R is 2-ethylhexyl.

8. Composition according to any preceding claim, wherein the composition is an oral composition and comprises an orally acceptable carrier.

9. Composition according to any preceding claim, wherein the composition is selected from the group consisting of pastes, gels, foams, liquids, powders and chewing gums and is suitable for use in dental care.

10. Composition according to any preceding claim, wherein the pH of the composition is from 7.5 to 12.

11. Composition according to any preceding claim, wherein the pH of the composition is from 8 to 11.

12. Composition according to any preceding claim, wherein the pH of the composition is from 9 to 10.

13. Composition according to any preceding claim, wherein the composition comprises chalk as abrasive.

14. Composition according to any preceding claim comprising a bicarbonate.

INTERNATIONAL SEARCH REPORT

Ir onal Application No
PCT/EP 02/09168

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K7/24

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, PAJ, WPI Data, CHEM ABS Data, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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"A" document defining the general state of the art which is not considered to be of particular relevance

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Date of the actual completion of the international search	Date of mailing of the international search report
3 February 2003	07/02/2003

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Lindner, A

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INTERNATIONAL SEARCH REPORT

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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